An Integrated Assessment Framework for Climate Change and Infectious Diseases

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Many potential human health effects have been hypothesized to result either directly or indirectly from global climate change. Changes in the prevalence and spread of infectious diseases are some of the most widely cited potential effects of climate change, and could have significant consequences for human health as well as economic and societal impacts. These changes in disease incidence would be mediated through biologic, ecologic, sociologic, and epidemiologic processes that interact with each other and which may themselves be influenced by climate change. Although hypothesized infectious disease effects have been widely discussed, there have not yet been thorough quantitative studies addressing the many processes at work. In part this is because of the complexity of the many indirect and feedback interactions or mechanisms that bear on all aspects of the climate issue. It also results from the difficulty of including the multitude of always-changing determinants of these diseases. This paper proposes a framework for an integrated assessment of the impacts of climate change on infectious diseases. The framework allows identification of potentially important indirect interactions or mechanisms, identification of important research gaps, and a means of integrating targeted research from a variety of disciplines into an enhanced understanding of the whole system. *Key words*: climate change, infectious disease, integrated assessment, multidisciplinary framework, vector-borne disease. *Environ Health Perspect* 107:329–337 (1999). [Online 23 March 1999]
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Many potential human health effects have been hypothesized to result either directly or indirectly from climate change, including heat-related illnesses; spread of infectious diseases; increases in the incidence of skin cancer; respiratory disorders; malnutrition; and population displacement from rising sea level. Changes in the prevalence and spread of infectious diseases are frequently cited potential effects of climate change. Such changes would be mediated through biologic, ecologic, sociologic, and epidemiologic processes that interact with each other and which may themselves be influenced by climate change. Changes in the rate of infectious diseases could have significant consequences for human health as well as economic and societal impacts. Although hypothesized infectious disease effects have been widely discussed, there have been only a few bounded quantitative studies, lesser in scope and detail than studies of other hypothesized climate change impacts such as agricultural productivity or sea level rise. This is due to the complexity of the many indirect and feedback interactions or mechanisms, driven by a multitude of always-changing disease determinants. This paper proposes an integrated assessment framework for this issue, allowing identification of potentially important indirect mechanisms, identification of important research gaps, and a means of integrating targeted research from a variety of disciplines. This paper also provides a review of key literature in the context of the framework.

Background

Climate change. Weather is defined as the "large fluctuations in the atmosphere from hour-to-hour or day-to-day" (*1*); climate is the "average weather, described in terms of the mean and other statistical quantities that measure the variability over a period of time and possibly over a certain geographical region" (*1*). Typical measures of climatic factors include long-term averages and natural variability in meteorological variables such as temperature and precipitation. Changes in climate are always occurring because of natural factors; often the term climate variability is used to refer to this natural component. Above and beyond this natural change there is superimposed the anthropogenic or human-induced component of climate change. In assessing the current state of knowledge about the potential effects of human-induced climate change, it is critically important to understand these different phenomena of weather and climate variability. Climate change encompasses temperature changes on global, regional, and local scales, and also changes in the mean and variability of rainfall, winds, and possibly ocean currents. In this paper, the term "climate change" is used to refer to weather variability, natural climate variability, and human-induced climate change.

Computerized general circulation models (GCMs) have been used to estimate the magnitude and extent of climate change on global and regional levels. However, there is little consensus among the results from different GCMs regarding changes at levels more detailed than global mean temperature. Assuming a doubling of the concentration of greenhouse gases from preindustrial levels, high latitudes are expected to warm by 3–5°C over the next hundred years, while low latitude temperatures may increase by 0.5–1.5°C (*1*). The global mean temperature increase for this scenario is estimated to be approximately 2.5°C by the end of the next century. Although these values are small compared with daily or seasonal fluctuations in temperature, changes of only a few degrees in global average temperature appear able to produce dramatic effects, depending on how they are realized.

Because of the large uncertainties about regional and local effects in regard to both the amount and the direction of change, it is difficult to predict the effects of human-induced climate change on human health. Nevertheless, many useful insights can be gained by exploring what might be the health implications of hypothesized climate changes and how these health effects might be ameliorated or avoided.

Infectious diseases. There are substantial differences between developed and developing countries in the incidence of various diseases. Over 40% of the population of the developing world, but only 2% of the developed world, is infected with at

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least one infectious or parasitic disease (*2*). This wide disparity is mainly related to differences in socioeconomic conditions, including nutrition, sanitation, housing, working conditions, and availability of health care. Both developing-world and developed-world populations may experience increased rates of various infectious diseases if the climate changes. Although the ability of wealthier countries to afford public health programs adds a substantial degree of protection, potentially significant risks also may exist for warmer parts of the industrialized world (*3*).

The world's major vector-borne diseases are shown in Table 1. The diseases most often cited as potential adverse consequences of climate change are dengue fever (typically transmitted by *Aedes aegypti* mosquitoes) and malaria (typically transmitted by *Anopheles* mosquitoes). Current qualitative estimates (*4*) suggest a substantial likelihood of both diseases spreading into susceptible, previously uninfected populations as the global climate warms. Table 1 indicates that there are a number of other diseases that have received less attention but are likely to change in prevalence and range with climate change. In Table 1, the rankings for likelihood of spreading took into account only a few of the many factors affecting the potential spread of these diseases. Changes in sociologic, ecologic, and climatic factors, and associated indirect and feedback mechanisms, are complex and often poorly understood. For example, increasing socioeconomic levels can lead to improved sanitation, reducing breeding sites for mosquitoes, but at the same time can involve the clearing of forests, resulting in increased contact between humans and vectors.

Several workshops and meetings have taken place in the last few years that underscore the broad transdisciplinary nature required for studying climate change issues. For example, a 1997 workshop conducted by the Washington Advisory Group (*5*) brought together a number of participants to identify research gaps and develop a proposed research agenda for climate change and infectious diseases, as follows (not in priority order):

- Climate modeling
  - Continue to improve regional climate analyses and models at the spatial and temporal scales appropriate for projecting the climate variables most useful to research on the health impacts of climate change
- Ecosystem dynamics and habitat alteration
  - Relate the biology of pathogens and vectors to ecosystem dynamics at various time scales (e.g., seasonal, interannual, and the scale of plant–community succession)
  - Determine how habitats (land, fresh water, and marine) are altered by climate change
  - Determine how habitat alteration and the consequent changes in ecosystem dynamics affect the biology of pathogens and vectors
- Disease surveillance
  - Improve mortality and morbidity surveillance for selected diseases, including active surveillance with laboratory confirmation in areas of special interest
  - Improve methods for detecting pathogens in vectors and in the environment
- Technologies for disease prevention and mitigation—assess existing technologies and develop new ones, such as:
  - vaccines
  - more effective, sustainable approaches for vector control
  - rapid methods for field diagnosis of disease
  - genetic techniques for identifying vectors and pathogens
- Disease transmission dynamics
  - Elucidate the biological, biophysical, and biochemical interactions among pathogens, vectors, and hosts that influence disease transmission
  - Develop disease transmission models that accurately incorporate these complex interactions
- Data sets for empirical studies—develop cross-disciplinary observation systems and the approaches and policies for data management that will:
  - link climate, health, and ecology data by employing new integrated approaches, such as geographical information systems
  - provide easy access to quality-controlled data
  - ensure compatibility and consistency over all time scales
  - enable the mining of historical direct and proxy data sources to extract priority variables
- Integrated assessments
  - Integrate health and climate indicators, socioeconomic changes, and technological changes in assessment models
  - Apply these integrated models to project scenarios for alternative futures
  - Develop strategies for cost-effective intervention and study their consequences for alternative scenarios
  - Seek improved methods for valuation and aggregation of health effects and other effects of climate change
- Capacity to detect, understand, and respond to surprises (unexpected events)
  - Improve the capacity for early detection, understanding, and effective response to unexpected emergence of disease, increased disease incidence, or nonlinearities in ecosystem dynamics and climate.

Table 1. The world's major vector-borne diseases ranked by population currently at risk

Disease	Causative agents	Vectors	Population at risk (millions)	Population infected (millions)	Likelihood of altered distribution with climate change
Dengue fever	Viruses	Mosquitoes	2,500	50/year	++
Malaria	Protozoa	Mosquitoes	2,400	300–500/year	+++
Lymphatic filariasis	Nematodes	Mosquitoes	1,094	117	+
Schistosomiasis	Flatworms	Water snails	600	200	++
Leishmaniasis	Protozoa	Sandflies	350	12	+
River blindness	Nematodes	Blackflies	123	17.5	++
Trypanosomiasis (sleeping sickness)	Protozoa	Tsetse flies	55	0.25–0.3/year	+

Abbreviations: +, likely; ++, very likely; +++, highly likely. Data from the World Health Organization [from McMichael et al. (*4*)].

Integrated assessment framework. A new integrated assessment framework (IAF) is presented in Figures 1 and 2. The objective of the framework is to identify the key plausible links and interactions that may influence the potential effect of climate change on diseases. Climate change is conceived as manifesting itself in each of three interrelated modules: changes in transmission biology, ecologic changes, and sociologic changes (links 1–3 in Fig. 1). These modules impact epidemiologic outcomes, including mortality and morbidity rates. Figure 2 captures some of the detailed direct and indirect interactions among the modules. Any effects of climate change will probably operate on the groups of factors in different ways and will likely be nonlinear, region specific, and time dependent. In both figures, the numbers on the arrows denote important transdisciplinary influences or causal relationships. The thick arrows in Figure 2 (links 4–7) represent aggregations, where multiple factors within a module may influence multiple factors within another module. The IAF can be used to help identify key gaps in our understanding of the various factors.

For example, climate change may alter the range and abundance of species present

in an ecologic community. Nutrient cycle changes, community relocation, and biodiversity loss may each affect vector physiology and behavior (such as host-seeking characteristics and biting rates), vector populations (by increasing or decreasing birth or death rates), and vector migration (by changing availability of suitable habitats). Similarly, the ecologic factors may each directly influence pathogen dynamics for nonvector-borne diseases. For vector-borne diseases, the predation rate on vectors may be altered, as may the availability of intermediate hosts for directly transmitted pathogens. Another example is that the demographic and economic effects of disease emergence could impact local ecosystems through pollution and habitat loss, which in turn could alter nutrient cycles and deplete species diversity. These effects may also arise from, or be exacerbated by, human migration. As a result, the ability of a local environment to supply nutritional needs may change over time (link 7), thus altering people's ability to combat disease. The IAF takes into account this feedback loop, where changes in the incidence of disease spark social and economic changes, which may impact ecologic dynamics, cascading back into the dynamics of the disease itself. Whereas some feedback loops may operate in a positive fashion, reinforcing a deleterious effect, we expect others to operate negatively, dampening effects among modules.

The IAF identifies many pathways through which climate change may affect infectious diseases. Some of these factors may be more important than others; the IAF does not identify which factors are most critical. It is likely that the critical pathways or mechanisms may differ depending on the particular disease and/or climate scenario under consideration. In addition, it is essential to consider the role of time. Because human-induced climate change, if realized, is expected to occur decades into the future, applying the IAF requires understanding of the sociologic, ecologic, biologic, and epidemiologic context in this future time frame and ensuring that this context is consistent with the corresponding climate assumptions. Of course, it is difficult to predict future changes, so the IAF is designed to incorporate models of the better known processes while accommodating a variety of scenarios for other factors.

Literature Review

There is a great deal of research addressing many aspects of current and emerging infectious diseases, ranging from anecdotal works to case studies of epidemics to detailed models of vector physiology. However, research into the effects of climate change on infectious diseases is still in its very early stages. Tables 2 and 3 summarize some of the key studies within the context of the IAF, clearly identifying which factors have and have not been explicitly considered. Because the body of literature encompassed by the framework is large, the literature summarized here is limited to selected studies that either directly address climate change impacts on infectious diseases (arrows 1–3, Fig. 1), or that address one or more of the interdisciplinary IAF links (arrows 4–13, Fig. 2). Outside the scope of this review is the larger body of literature addressing specific single-discipline issues, such as the physiology of specific vectors, the effectiveness of mosquito control programs, or the effect of economic development on the susceptibility of the population. Although these studies would likely have a direct bearing on the magnitude of potential disease impacts, they were not framed specifically either in the context of climate change or interdisciplinary links.

Table 2 categorizes papers by whether they are review articles or original research, by type of research conducted, and by aspects of the issue covered. Because malaria and dengue fever have been the focus of a great deal of the climate-related literature, the table notes articles that relate to these diseases. The summary totals for malaria and dengue reflect the pattern in the rest of the literature: approximately half of the papers are reviews and half are original quantitative research. Most of the research papers focus on field data from particular regions, and include some kind of statistical analysis. Sixteen of the 33 papers contain structural mathematical

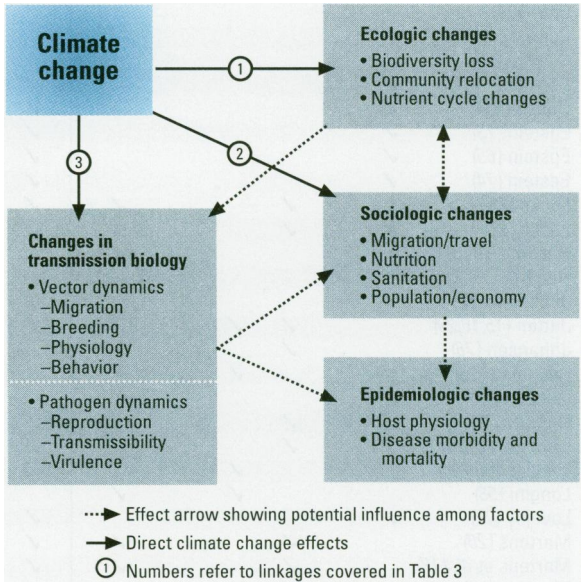

Figure 1. Integrated assessment framework for evaluating research on the association between climate change and infectious diseases. See Figure 2 for detailed links 4–13.

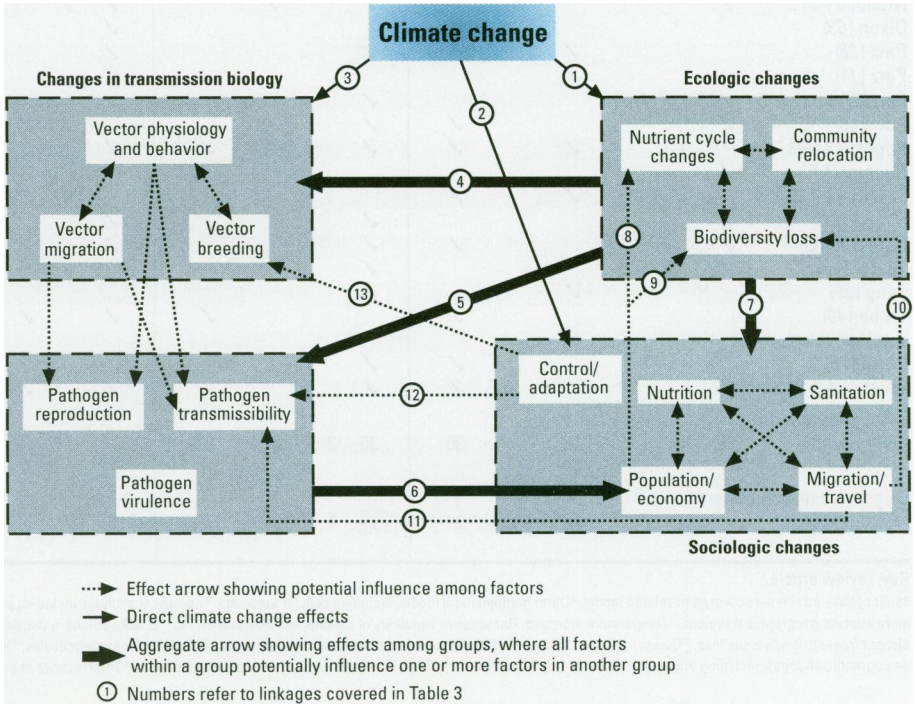

Figure 2. Details of integrated assessment framework links among ecologic, sociologic, and biologic factors.

Table 2. Summary of how the literature on climate change and vector-borne diseases covers the subject areas in Figure 1. Only those papers that relate to climate influences are included

First author (reference)	Rev	Model					Climate change				Biologic			Ecologic			Sociologic				
		SIR[a]	OM[b]	Stat[c]	Lab[d]	Reg[e]	T[f]	s_C[g]	ENSO[h]	Other	V[i]	P[j]	H[k]	BD[l]	CR[m]	NC[n]	Tvl[o]	Nutr[p]	San[q]	Pop[r]	m/d[s]
Abisudjak (*56*)						✓					✓		✓		✓		✓				m
Ault (*52,61*)	✓																				m
Anderson (*68*)	✓	✓				✓					✓	✓	✓		✓						m/d
Bouma (*7*)				✓		✓	✓	✓	✓		✓										m
Bouma (*9*)				✓		✓			✓												m
Bradley (*14*)		✓	✓	✓		✓	✓				✓						✓				m/d
Burgos (*69*)				✓		✓	✓				✓				✓						m
Cheesbrough (*70*)				✓	✓	✓				✓		✓									
Chen (*71*)	✓																✓			✓	
Coluzzi (*48*)	✓					✓					✓			✓	✓						m
Colwell (*30*)	✓											✓									
Cook (*72*)	✓						✓				✓	✓						✓	✓		m
Dobson (*34*)	✓						✓				✓	✓	✓		✓						m
Epstein (*73*)	✓						✓		✓			✓			✓						
Epstein (*65*)	✓						✓		✓			✓			✓						
Epstein (*74*)	✓						✓	✓	✓		✓	✓		✓	✓	✓	✓		✓		
Focks (*26*)			✓			✓	✓				✓										d
Focks (*27*)	✓		✓			✓	✓				✓										d
Herrera-Basto (*24*)					✓	✓							✓						✓		d
Huq (*31*)					✓		✓			✓											
Jackson (*75*)	✓						✓	✓	✓		✓	✓									m/d
Jetten (*15,16,29*)			✓	✓		✓	✓				✓										m/d
Johansen (*76*)			✓									✓	✓								
Koopman (*23*)				✓		✓							✓						✓		d
Lainson (*49*)	✓					✓					✓	✓			✓		✓				
Lindsay (*12*)	✓		✓				✓			✓	✓										m
Lindsay (*13,21*)			✓				✓			✓	✓										m
Loevinsohn (*10*)				✓		✓	✓						✓								m
Longini (*58*)				✓		✓							✓				✓				
Lovejoy (*77*)	✓						✓				✓		✓		✓						
Martens (*20*)			✓			✓	✓						✓								m
Martens et al. (*18*)			✓			✓	✓						✓								m
Martens (*66*)			✓							✓											
Martin (*19*)			✓				✓						✓				✓				m
Meek (*60*)	✓					✓					✓		✓				✓				m
Morse (*78*)	✓					✓			✓		✓		✓								
Newton (*79*)		✓									✓										d
Nicholls (*42*)	✓						✓		✓		✓	✓									
Olson (*63*)					✓						✓										d
Patz (*28*)				✓			✓				✓										d
Patz (*11*)				✓						✓	✓										m
Patz (*67*)	✓						✓														
Patz (*80*)	✓					✓	✓		✓		✓	✓	✓					✓			m/d
Rogers (*37,38*)				✓		✓	✓			✓	✓										
Roundy (*54*)	✓																✓				m
Sattenspiel (*59*)		✓		✓		✓							✓				✓				
Shope (*81*)	✓						✓				✓										d
Sutherst (*39*)	✓					✓	✓				✓										m
Tester (*46*)	✓						✓					✓									
Tong (*35*)				✓			✓														
Trape (*40*)						✓				✓	✓		✓								
van Herwaarden (*82*)			✓	✓																	
Ward (*25*)						✓	✓				✓										d
Wilson (*47*)	✓					✓	✓				✓		✓				✓			✓	
Total papers (no.)																					
By category[t]	26	4	15	18	4	30	35	3	9	10	35	14	18	2	10	1	11	2	4	2	22m 14d
Original research papers (no.)																					
By category[u]	–	3	13	18	4	21	19	1	2	9	18	2	11	0	2	0	4	0	2	0	12m 8d

Rev, review article.

[a]Susceptible–infected–recovered or related model. [b]Other mathematical model, including cellular automata. [c]Statistical analysis, including probability and simulation. [d]Laboratory model. [e]Model focusing on one or more specific geographical regions. [f]Temperature increase. [g]Increase in variability of climate, extreme events, etc. [h]El Niño Southern Oscillation. [i]Vector dynamics. [j]Parasite dynamics. [k]Host population dynamics (as distinct from *r*). [l]Biodiversity loss. [m]Community relocation, including expansion of previously rare pathogens. [n]Alteration of nutrient cycles. [o]Human travel and migration. [p]Human nutrition. [q]Human sanitation. [r]Human demographic changes, including population increase (as distinct from *k*). [s]Malaria and/or dengue fever as specific focus. [t]Total number of papers 59. [u]Total number of original research 33.

models; only four are laboratory studies. Table 3 focuses on linkages; specifically, climate-change influences and interdisciplinary linkages. The studies are mapped to links in the IAF shown in Figures 1 and 2. No single study covers all links, and there are several links in Figure 2 (links 2, 5, 7–10, 12) for which we were unable to identify any relevant literature. Although there have been some efforts to estimate the direct impact of increasing temperatures on transmission biology, comparatively little work has been done to integrate climate-related ecologic and sociologic factors. In this paper we will review the associations between climate factors and ecologic and sociologic factors influencing diseases.

Climatic factors influencing diseases. There is a substantial amount of literature relating weather and climate and their relationships to particular diseases, but not considering climate change per se. Many studies, however, have clear implications for climate change effects and could be adapted to explore different scenarios. The effects of temperature and other meteorological variables on the physiology of some disease vectors have been known for quite some time [see Gillett (*6*) for one of many examples of this material] so only recent work is reviewed here. Because malaria and dengue fever have been the most extensively studied, these diseases are reviewed individually, followed by a brief summary of research on other diseases.

Malaria. For malaria, several associations with higher temperatures or climatic events have been reported in recent years. For example, Bouma et al. (*7,8*) showed that malarial occurrence in Pakistan has increased in regions experiencing higher minimum temperatures since the late 1980s. Bouma et al. (*9*) showed a strong relationship between the incidence of malaria in Colombia and the occurrence of the El Niño Southern Oscillation. Loevinsohn (*10*) showed how record high temperatures and rainfall in Rwanda caused malaria to emerge and persist at unusually high altitudes. Patz et al. (*11*) used soil moisture modeling to predict *An. gambiae* biting rates and subsequent entomologic inoculation rates in Kenya. Lindsay and Birley (*12*) examined the relationship between temperature and vectorial capacity of *An. maculipennis*, a European malaria vector, and also reviewed various modeling approaches. Lindsay et al. (*13*) used geographical information systems and a regression approach to develop relationships between climatic variables and the relative abundance of two African malaria vectors.

Models to explore malaria under climate change scenarios take a variety of approaches. Bradley (*14*) estimated temperature sensitivity of factors driving the number of secondary infections produced by introducing an infectious individual into a population of susceptibles (R_0). He found that changes in the extrinsic cycle of the *Plasmodium* protozoan could raise R_0 in many currently nonmalarious areas to a point where malaria might take hold. Jetten and Takken (*15*) and Jetten et al. (*16*) predicted that infections in southern Europe could increase dramatically, using a simulation model incorporating anopheline physiology and climate-change scenarios. Using a similar approach, Haile (*17*) predicted how malaria might spread in the United States under modified weather conditions and concluded that it was not likely in areas other than Florida.

Martens et al. (*18*) focused on mosquito survival probabilities, biting frequency, and extrinsic incubation period, and developed a model for the epidemic potential for *P. vivax* and *P. falciparum* as a function of temperature. They used this information in conjunction with temperature projections from a GCM to estimate how worldwide malaria distributions might change. Martin and Lefebvre (*19*) calculated a malaria occurrence zone from generic information about the temperature requirements of the mosquito species that transmit malaria. Both studies predicted that the most pronounced increases in malaria would be at the borders of endemic areas and at higher altitudes. In a separate study, Martens (*20*) attempted to quantify mitigation efforts by developing a new index to measure the sustainability of malarial spread. This index incorporated three important components [rate of temperature change; change in the disease burden on human populations; and economic factors, measured by the ratio of the rate of gross national product growth to the rate of population growth] to estimate disability-adjusted life-years (DALYs) lost per year under various portfolios of energy sources. Although the areas of low endemicity showed the greatest increase in DALYs lost per year [supporting the conclusions of Martens et al. (*18*) and Martin and Lefebvre (*19*)], the greatest disease burden still lay in poor tropical countries where *P. falciparum* is most prevalent and mitigation efforts are mostly inadequate. These studies shared similar conclusions, predicting that a global average 2°C rise in temperature could cause permanent malaria to expand to higher altitudes in the tropics and subtropics (up to nearly 2,000 m in some regions), and that seasonal malaria could be found in some temperate regions as far north as northern Europe. Lindsay and Martens (*21*) applied these concepts along with regional climate change predictions to estimate epidemic potential in Zimbabwe. The studies by Martens et al. (*18*) and Martens (*20*) are among the first examples of truly integrative work to understand the problem of climate change and infectious disease. But, as can be seen from Table 2, more integrative steps are needed to better understand the potential for spread of malaria.

Dengue fever. Watts et al. (*22*) found that the transmission efficiency of dengue virus by *Aedes* mosquitoes in the laboratory was higher at higher temperatures, which explains seasonal variations in Bangkok. Using a serosurvey, Koopman et al. (*23*) identified median temperature in the rainy season as the strongest predictor of dengue transmission in Mexico. Field studies have reported altitudinal and latitudinal shifts in disease prevalence similar in direction and magnitude as for malaria. Herrera-Basto et al. (*24*) reported dengue fever climbing from 1,200 to 1,700 m above sea level in Mexico, in areas where the vector but not the disease had been previously present. They emphasized that local climatic conditions were more important in predicting outbreaks than elevation per se [see also Koopman et al. (*23*)], but the implication was that climate change may assist the spread of dengue into new susceptible areas. Ward and Burgess (*25*) examined the possibility for latitudinal spread of dengue by estimating the shift of 0°C isotherms (the minimal conditions for overwintering of eggs and larvae), and concluded that much of central and southern Europe could be at risk.

Focks et al. (*26,27*) developed a weather-driven model to simulate life-table information for *Ae. aegypti* (called CIMSiM) and a dengue simulation model (DENSiM). Both models focused on vector dynamics and have been parameterized with field data with a view toward informing the design of vector control strategies. Focks et al. (*26,27*) validated the DENSiM model in some locations, e.g., Honduras, where the DENSiM model simulations accurately predicted actual disease incidence. Patz et al. (*28*) used CIMSiM and DENSiM in conjunction with GCMs to predict the increased dengue epidemic potential in five selected cities, as well as the increased global epidemic potential. Jetten and Focks (*29*) examined the critical mosquito density for dengue fever [which is defined as the inverse of what Martens (*18,20*) calls the epidemic potential] and related it to temperature change to quantify the influence of global warming on the intensity and distribution of dengue. Temperature influenced adult survival, length of the gonotrophic cycle, extrinsic

incubation period, and vector size (which directly influences biting rate). The authors projected an increase in the latitudinal and altitudinal range of dengue as well as increased duration of the transmission season in temperate locations. Because immature *Ae. aegypti* mosquitoes suffer pronounced mortality above 42°C, if climate warming increases daily peaks substantially, then the incidence of dengue may decline in the hottest parts of its current range.

Other diseases. Cholera is a typically waterborne disease, with outbreaks often related to floods or droughts. A series of influential papers may explain the origins of cholera outbreaks. Colwell and Huq (*30*) discovered that cells of *Vibrio cholerae* are able to enter a state of dormancy in response to nutrient deprivation, elevated salinity, or reduced temperature. When these cells emerge from dormancy under appropriate conditions, such as increased water temperatures from El Niño events, they may attach themselves to the copepods (zooplankton), as demonstrated by Huq et al. (*31*). The combined effect of *V. cholerae* emergence and zooplankton blooms in warm nutrient-enriched waters has been hypothesized to concentrate the cholera pathogen in waters close to human settlements (*30*). However, many other factors also may be involved. The Latin American epidemic of 1991–1993 may have been triggered by container ships from Asia emptying their sewage or ballast water into the sea around Lima during an El Niño period, although this has never been confirmed (*32*). This highlights the interconnectedness of physical, biologic, and sociologic processes.

Dobson and Carper (*33,34*) reviewed host–parasite and disease–vector relationships from an ecologic perspective, and suggested that under global warming, shorter development times could change the range of previously rare or extreme-temperature pathogens. Tong et al. (*35*) noted a relationship between temperature, humidity, and rainfall and the incidence of Ross River virus. Reeves et al. (*36*) investigated the temperature responses of the mosquito *Culex tarsalis* to global warming scenarios in California, and showed that the range and prevalence of St. Louis encephalitis and western equine encephalitis could change. Haile (*17*), using a numerical simulation model, predicted that the American dog tick, *Dermacentor variabilis*, which carries Rocky Mountain spotted fever, might become extinct in the southern parts of its range because of excessive temperature and low humidity predicted under global warming. Rogers and Randolph (*37*) and Rogers and Packer (*38*) correlated the presence and absence of vectors at specific locations in tropical Africa with indices of vegetation cover and temperature to predict how their geographical distributions may shift under climate change scenarios. Sutherst (*39*) incorporated the temperature and moisture requirements of a species into a model to investigate the impacts of climate change on the distributions of vectors. Regional results were quite dramatic. For example, under a scenario of a 1°C rise in temperature per 10° latitude, a 20% increase in summer rainfall, and a 10% decrease in winter rainfall in Africa, *Glossina palpalis*, a tsetse fly that transmits trypanosomes, could migrate far into South Africa, putting millions of people in major population centers at risk. When applied to vectors for malaria and dengue, the same scenario gave slight increases in abundance of mosquitoes at higher latitudes, and a substantial increase in Europe.

Trape et al. (*40*) carried out a field study which suggested that the persistence of the sub-Saharan drought from 1970 to 1992 allowed tick vectors to colonize new areas in West Africa and was the probable cause for a considerable spread of tick-borne borreliosis. The opposite weather extreme of flooding also may impact rates of infectious diseases. The Centers for Disease Control and Prevention (*41*) noted an association between hurricanes, with their torrential rainfall, and leptospirosis. Nicholls (*42*) cited evidence that increased climatic variability might lead to increased frequency and/or intensity of epidemics of arboviral diseases; for example, Murray Valley encephalitis in Australia (*43,44*). Schoental (*45*) suggested that under warmer conditions, fungi could increase in number and could release mycotoxins with toxic, immunosuppressive, teratogenic, or carcinogenic compounds. Tester (*46*) described research showing how global warming might lead to decreased atmospheric circulation and ocean mixing, resulting in dinoflagellate blooms. In a review on Rift Valley fever, Wilson (*47*) traced the roles of environmental change (especially unusual rainfall), ungulate migrations, economic development, human demography, behavior, and travel on the dynamics and distributions of *Aedes* and *Culex* mosquito vectors, resulting in changes in endemic prevalence, epidemic frequency, and epidemic intensity.

Ecologic and sociologic factors influencing diseases. In addition to the direct climatic influences described above, there is widespread recognition that climate can affect ecologic and sociologic processes and factors, which in turn may affect disease prevalence. What is known is rather fragmentary and clearly indicates the complexities that need to be considered. Some studies shed light on both disease emergence and opportunities for integration with climate change via the links in the IAF. It is not intended that the following examples represent a complete list of such studies; rather, they are a sample covering ecologic change, economic development, migration and travel, and adaptation and control. In contrast to the disease-focused research previously reviewed, most of the literature on ecologic and sociologic factors is targeted to specific factors or linkages.

Ecologic change. Ecologic changes can affect many of the biologic and sociologic factors influencing rates of vector-borne diseases (links 4, 5, and 7 in the IAF). Most studies of ecologic change and infectious diseases concern habitat loss. Coluzzi (*48*) investigated ecologic damage as a driver of malaria patterns; Lainson (*49*) focused on how habitat destruction has changed the incidence of leishmaniases in Amazonian Brazil; and Spielman (*50*) and Komar and Spielman (*51*) studied how Lyme disease and eastern encephalitis responded to habitat and landscape changes in New England. Ecologic changes such as nutrient cycle disruption from pollution and biodiversity loss usually receive a cursory treatment in reviews on disease emergence.

Economic development. Economic development relates to interdisciplinary factors in the IAF through links 8 and 9. The impact of economic development on sociologic factors, such as nutrition and sanitation, are critical when considering the potential effects of human-induced climate change on health, but are beyond the scope of this review. Ault (*52*) focused on the relationships between population growth, agricultural intensification, and malaria. High human birth rates result in agricultural intensification and land use changes, potentially altering breeding sites for malarial mosquitoes. Ault (*52*) argued that the eradication of malaria in developing countries could be achieved in conjunction with economic development driven by population growth. By contrast, Brinkmann (*53*) argued that the increased polarization of societies from economic growth could favor the transmission of diseases because the poor would become more marginalized.

Dam-building associated with economic development may have significant effects on vector-borne diseases, with reservoirs serving as breeding grounds that can increase populations of vectors sometimes 10–100-fold (*54*). Dam-building also often requires resettlement programs that serve to transport diseases to new places as people and animals, as carriers and hosts, relocate. Under global climate change, not only might water temperatures in reservoirs increase, resulting in faster breeding times for mosquito vectors,

but changes in reservoir levels also could alter the breeding sites in the shallow fringes.

Migration and travel. Human migration and travel plays a major role in disease spread [see Wilson (*55*) for a comprehensive review]. Its potential interdisciplinary impacts on ecologic and biologic factors are shown as links 10 and 11 in the IAF. In Indonesia, for example, a wide variety of diseases (malaria, dengue hemorrhagic fever, filariasis, chikungunya, Japanese encephalitis, scrub typhus, and schistosomiasis) have been spread among susceptible populations by transmigration combined with, and exacerbated by, the clearing of forests (*56*). Kondrashin and Orlov (*57*) cited examples of disease spread from people traveling for work, tourists, transport workers, military personnel, and refugees.

Although few in number, quantitative model-based studies of mobility sometimes predicted disease emergence with considerable accuracy. Longini et al. (*58*) studied the mobility of people among two dozen major urban regions, then applied the resulting model to data on the influenza pandemic of 1968–1969 at the scale of the former Soviet Union and the world. The model predictions fit the historical spread very closely. Sattenspiel and Dietz (*59*) achieved a similar level of accuracy using a model adapted to include host mobility, applied to a measles outbreak in Dominica. Although regular travel may or may not increase as a result of climate change, there is a possibility that refugee migrations will, as people move away from areas that become unproductive. The temporary nature of most refugee camps, however, may make them less significant in changing vector-borne disease patterns than permanent population relocations related to agriculture and other development (*60*).

Adaptation and control. There are many measures to adapt to and control infectious diseases (IAF links 12 and 13). Ault (*61*) argued that the control of malaria usually focuses on identification and treatment of human populations and control of vectors and may miss important social and demographic components, including reducing the risk of exposure; reducing the forces that increase the numbers of people at risk, e.g., habitat loss and migration; and making mitigation efforts more sensitive and responsive. In addition to climatic, ecologic, and sociologic effects, Gubler and Clark (*62*) maintained that the spread of dengue fever in Latin America after 1970 also was due to the belief in the health community that the disease was under control and the consequent discontinuance of a concerted *A. aegypti* eradication effort.

In addition to vector control, infectious diseases are being combated at the molecular level. Olson et al. (*63*) reported genetically engineering resistance to the transmission of the dengue virus in *Aedes* mosquitoes by making it impossible for the virus to enter the salivary glands. This raises the possibility that vector-borne diseases may be controllable simply by altering the genetic structure of the vectors. However, many disease agents may eventually evolve around such genetically engineered defenses, and there are unknown consequences of releasing genetically engineered species into ecosystems.

Discussion

The IAF presented in this paper provides a means by which cross-disciplinary research could be integrated to identify, target, and initiate investigation in a number of areas, including: systematic understanding of ecologic and epidemiologic responses to climate changes; potential effects of climate changes on food and water supplies; effects of resource availability on human demographic changes (e.g., migration, urbanization), and vice versa; confounding effects of travel, habitat loss, and pollution; potentially mitigating effects of increasing wealth, sanitation, nutrition, and disease control, or divergence in standards of these among human populations; effects of human activities on ecosystems; and urbanization and patchy or heterogeneous dynamics.

The task of understanding and modeling the linkages does not necessarily involve gathering entirely new information; rather, a large portion of the task is to integrate what is already known from a wide variety of disciplines. The Table 3 categorization of the literature shows it may be possible, particularly for the tropics, to develop preliminary models or estimates for links 1, 3, 4, 6, 11, and 13 in relation to climate change scenarios. One problem with link 1 between climate change and ecologic changes is that little is known with any reliability on a regional level. The precise effects of ecologic changes on vector and pathogen dynamics will depend on the mix and relative abundance of other species in a community. There is a sizable literature on ecologic effects on pathogens (not covered in detail in this review) that addresses link 5. Links 7–10 are the concern of geographers, human ecologists, and conservation biologists. Collectively, these groups are able to provide crude estimates of the potential effects of human sociosystems and ecosystems on each other [for example, the data in *World Resources 1993–1994* (*64*)]. Link 12 is addressed in the public health literature and, although Table 3 does not show any studies that relate this to climate change, there is substantial literature on the effectiveness of pathogen control programs. The IAF does not indicate which of these links is most important under different scenarios per se, but does provide a means to target research.

An overarching need exists for transdisciplinary studies that integrate the various factors. Studying one or two processes in isolation does not give a reliable picture of the potential climate-induced change in the range of a disease, given the feedbacks and interactions among the various systems. A truncated understanding, excluding indirect or feedback effects, may lead to highly erroneous conclusions. On the other hand,

Table 3. Summary of how the surveyed literature covers the links in the integrated assessment framework in Figures 1 and 2

First author (reference)	Link 1	2	3	4	5	6	7	8	9	10	11	12	13
Dengue fever													
Jetten (*29*)			✓			✓							(✓)
Ward (*25*)			✓										
Patz (*28*)			✓										
Malaria													
Bouma (*7,9*)			✓										
Bradley (*14*)			✓										(✓)
Loevinsohn (*10*)			✓										(✓)
Martens (*18,20*)			✓			✓							✓
Martin (*19*)			✓										
Sutherst (*39*)[a]			✓										(✓)
Other diseases													
Komar (*51*)				✓									
Longini (*58*)											✓		
Rogers (*37,38*)	✓		✓	✓									(✓)
Sattenspiel (*59*)											✓		
Trape (*40*)			✓										
Wilson (*55*)[b]											✓		(✓)

Only original research is included. This table covers studies that directly address climate change and studies that address cross-disciplinary links in the framework. Check marks in parentheses mean that the author mentions or discusses an effect but does not provide a quantitative analysis.

[a]This author focuses primarily on malaria but also covers dengue.

[b]Review article containing many cited examples of link 11.

overbuilt integrated models can create a false sense of accuracy. This does not mean that every detail of every link must be fully understood before conclusions can be drawn; often, it may be necessary to use initial qualitative or crude quantitative models for a particular link until more research results are available. However, an acknowledgment of the full set of factors is necessary for an adequate representation of the system and identification of areas that are not sufficiently understood.

There have been a number of efforts to build integrated frameworks to characterize the effects of climate change on diseases (*52,53,65,66*). These frameworks are not disease specific, with the exception of Ault's (*52*) depiction of the malaria system in terms of biologic, ecologic, and sociologic factors. Ault's framework is not intended to guide integrated assessments. His framework achieves greater detail than the proposed IAF at the cost of generality to other diseases. Epstein (*65*) proposed a framework for an integrated assessment (IAS) consisting of a climate system, ecosystem, and social system, which jointly produce physical, biologic, and social indicators and outcomes. Epstein (*65*) characterized ecosystem vulnerability in terms of the stability of populations. The IAS has applicability beyond diseases per se and is intended to guide the design of assessment tools. The IAF framework is more restricted in that it intends to describe the links between climate change and infectious diseases, but goes into greater detail in this area than Epstein's framework. Brinkmann (*53*) put forward a set of influence diagrams (processes linked by cause–effect arrows, similar in structure to the IAF) to frame his discussion about economic development and tropical diseases. He covered sociologic factors, such as agricultural intensification, poverty, and development. These diagrams share a partial resemblance with the IAF, but the IAF covers a broader range of relationships.

The frameworks of Martens (*66*) were both influence diagrams and model descriptions. The MIASMA model is a multidisciplinary integration of models characterizing global atmospheric changes, human health, autonomous developments, and responses. It is part of an overall modeling framework called TARGETS, designed for sustainable development planning. Both MIASMA and TARGETS are more general than the IAF framework in terms of health effects and add greater resolution of sociologic effects. By contrast, there is no explicit depiction of ecologic effects; instead these are subsumed within a broader biophysical compartment. A similarly integrative framework was proposed by Patz and Balbus (*67*). It was designed for ecologically based human health risk assessment, and it develops integrated mathematical models based on historical analyses of climate change and disease data. Patz and Balbus' (*67*) approach incorporates less in the way of sociologic processes than other approaches, including the IAF.

The IAF presented in this paper is a new large-scale socioecologic model structure in which existing or newly developed models are applied to individual links or processes. This structure facilitates investigation of potential direct and indirect disease impacts resulting from particular climate change scenarios under a variety of local and regional assumptions. The framework can integrate the most recent research on each link as well as highlight the areas containing research gaps. The IAF provides the transparency required for detailed modeling as well as the transdisciplinary breadth required to address the issue.

Clearly, there remains a daunting challenge to successfully develop accurate models of the many interrelated epidemiologic, biologic, ecologic, and sociologic processes that affect the prevalence and spread of infectious diseases, and the effect of climate change on all of these factors. Because changes in infectious disease patterns and prevalence could be significant impacts of climate change, such an understanding is vital to make informed, intelligent policy decisions.

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